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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/632,735	08/04/00	BAEZA-RAMIREZ M	RG0107US (#9

HM12/0330

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 03/30/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/632,735	BAEZA-RAMIREZ, MARIA ISABEL	
	Examiner	Art Unit	
	Terri L Ivory - McCaa	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 January 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *6-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claims *1-31* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-5, drawn to a diagnosis method for determining an individual having clinical characteristics of primary and secondary antiphospholipid syndrome, classified in class 435, subclass 7.1.

II. Claims 6-10, drawn to a diagnosing kit for detecting anti-lipidic particles antibodies by utilizing antibodies conjugated to an enzyme and healthy individuals serum as a negative control, classified in class 435, subclass 7.72.

III. Claims 11-15, drawn to a diagnosing kit for detecting anti-lipidic particles antibodies by utilizing antibodies conjugated to fluorochromes and monoclonal antibody as positive control classified in class 436, subclass 546.

IV. Claims 16-21, drawn to a diagnosis kit for the direct detection of lipidic particles utilizing antibodies conjugated to a fluorochrome and enzyme and the sample is from organ tissue , classified in class 436, subclass 547.

V. Claims 22-25, drawn to a therapeutic method for treatment of individuals having primary and secondary antiphospholipid syndrome, classified in class 436, subclass 506.

VI. Claims 26-31, drawn to a method and kit for determining different cellular physiologic states in sample of cells, classified in class 436, subclass 63.

2. Inventions I and II-IV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are a method and kits. Group I is drawn to a method of diagnosing clinical characteristics of primary and secondary antiphospholipid syndrome while group II,III & IV are drawn to a kit for detecting anti-lipidic particles antibodies. These inventions are different because of they have different modes of operation, different functions and different effects therefore they are patentably distinct.

3. Inventions I and V,IV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are methods. Group I is a method for diagnosing clinical characteristics of primary and secondary antiphospholipid syndrome while group V is a therapeutic method for treatment of individuals having primary and secondary antiphospholipid syndrome and group VI is a method and kit for determining physiologic states in sample of cells. These inventions are unrelated because they have different modes of operation, different functions and different effects therefore they are patentably distinct.

4. Inventions II and III,IV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are kits. Group II is a kit which requires antibodies conjugated to enzyme as well as a negative control comprising serum from a healthy individual, group III is a kit which requires antibodies conjugated to fluorochromes as well as a positive control comprising monoclonal antibodies while group IV is a kit which requires antibodies conjugated to a fluorochrome and an enzyme and is capable of testing samples of organ tissue instead of serum. These inventions are unrelated because of their different modes of operation and different functions therefore they are patentable distinct.

5. Inventions II and V,VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are methods and kits. Group II is a kit for detecting anti-lipidic particles antibodies, group V is a method for treatment of individuals having primary and secondary antiphospholipid syndrome and group VI is a method and a kit for determining different cellular physiological states in sample of cells. These inventions are unrelated because of their different modes of operation, different functions and different effects therefore these inventions are patentably distinct.

6. Because these inventions are distinct for the reasons given above and the search required for one Group is not required for another Group and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

7. During a telephone conversation with Mr. Hochberg on 06 March 2001 a provisional election was made with traverse to prosecute the invention of group I, claims 1-5. Affirmation of this election must be made by applicant in replying to this Office action. Claims 6-31 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

8. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Specification

35 U.S.C. 112, first paragraph, requires the specification to be written in "full, clear, concise, and exact terms." The specification is replete with terms which are not clear, concise and exact. The specification should be revised carefully in order to

comply with 35 U.S.C. 112, first paragraph. Examples of some unclear, inexact or verbose terms used in the specification are: In the " field of inventions paragraph" the meaning of the term obtension is not known. Page 10 line 14 recitation of the phrase " make react with the cells" is not grammatically correct. There are also contradictions within the specifications such as page 12 lines 13-23. One paragraph discloses detection of the presence or absents of lipidic particles in a serum sample while the next paragraph discloses detection of antibodies in serum sample by using antigen lipidic particles. Examiner suggests that applicant review the translated specification in its entirety and correct any errors associated therewith. No new matter should be entered.

Drawings

9. Application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.

Information Disclosure Statement

10. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate

paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Claim Rejections - 35 USC § 112

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for liposomes and neoplastic cells, does not reasonably provide enablement for all lipidic particles recited in claim 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Page 12 line 30 of the specification discloses liposomes and neoplastic cells as antigen containing lipidic particles, however, the claimed method in claim 1 states that lipidic particles are to be detected from serum by a direct or indirect fashion and the results are to determine the diagnosis of primary or secondary antiphospholipid syndrome. Absent evidence to the contrary, Lipidic particles are always present in the serum in some type or form. Cholesterol such as LDL and HDL are lipidic particles, there are triglycerides found in serum which are lipidic particles, there are lipidic particles that may result from inflammation caused by different types of injuries or infections, there can be lipidic particles from T-cell destruction of cells or apoptotic cells.

These various types of lipidic particles circulate through out the blood stream, however, detection of these particles do not correlate to the recited diseases of claim 1 nor are they indicative of primary or secondary antiphospholipid syndrome. Therefore, It is not clear as to how the claimed method would be able to discriminate between miscellaneous lipidic particles and lipidic particles which are indicative of an antiphospholipid syndrome. As such, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

12. Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claimed method is for detecting lipidic particles in patient serum by a direct or indirect method by using a detection protocol. The recitation of the detection protocol is not sufficient to enable the claimed method, furthermore, the specification does not provide enablement for the detection of lipidic particles in serum as recited in claim 1. The specification page 12 line 30 states that the lipidic particles of the method are liposomes and neoplastic cells. Page 12, line 24-29 of the specification discloses a method for contacting lipidic particles which contain lipidic antigens to serum sample to detect any anti- lipidic antibodies present in the sample. This is not what is disclosed in the body of the claim but is suggested in the preamble of the claim.

Example 1 provides a protocol for an indirect detection by liposomal- ELISA method for lipidic particles through the detection of anti-lipidic particles antibodies in sera from patients. Claim 1 is enabled for the disclosure of example 1. As a starting point to correcting claim 1, applicant should consider incorporating the method steps exemplified in example 1 into the instant method.

Claim Rejections - 35 USC § 112

13. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is confusing because the preamble is directed to a diagnostic method for determining, in an individual, clinical characteristics of primary and secondary antiphospholipid syndrome, but the body of the claim does not recite any steps for diagnosing the clinical characteristics. Instead the claim recites detection of lipidic particles in serum from an individual by direct or indirect fashion, and that the presence of lipidic particles is indicative of development of a disease associated to the presence of antiphospholipid antibodies in the individual, but there is no correlation between the

detection of the antiphospholipid antibodies in the serum to diagnosis of either primary or secondary antiphospholipid syndromes recited in the preamble of the claim.

14. Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: Since the method requires detection of the binding complex , there needs to be some type of label for the complex. It is unclear as to how the lipidic particles or antibody complex can be detected. There needs to be an indication of what type of antibodies involved with the binding of lipidic particles to form a complex. There is no indication if this assay is homogeneous or if it may be heterogeneous and if it is heterogeneous there needs to be a substrate of some type.

15. Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: a contacting step, detecting step, and correlation step to correlate the presence of lipidic particles in a sample to the diagnosis of primary or secondary antiphospholipid syndrome.

16. Claim 1 provides for the use of a detection protocol, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process

applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

17. For the purposes of making an art rejection(s), in view of the 112 2nd rejections, the claims are interpreted as a method for detection of anti – lipidic antibodies or antiphospholipid antibody, in a patient serum, consisting of binding the serum antibodies to antigenic lipidic particles incorporated into liposomes, as disclosed in the specification.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

18. Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Maxfield Wilson et al USP 5776487.

Maxfield Wilson teaches a method for determining analyte in a test sample comprising contacting patient serum with a liposome reagent (antigen lipidic-particle) which is immobilized to a solid support surface. Detection of the amount of analyte is determined by labeling of the liposome or the analyte (Col. 2, Lines 45-65).

19. Claims 1,2,4&5 are rejected under 35 U.S.C. 102(b) as being anticipated by Stewart et al USP 5,840,587.

Stewart teaches forming phospholipid covered particles for the detection of antiphospholipid antibodies. Incubation of the human serum allows for binding of the antiphospholipid antibodies to the phospholipid covered particle. A second antibody with a detectable label is applied to the complex for detection (Col.4, lines 53-65). Stewart also discloses that the phospholipid covered particles may by utilized for specific antiphospholipid antibody production in animals. This suggests that the antibodies formed may be generated to form polyclonal and monoclonal antibodies (Col.7, Line 29 – 39).

Conclusion

20. Claims 1-5 are rejected. Claims 6-31 are withdrawn.

21. References: Matsuura et al USP 5506110;Maxfield Wilson et al USP 5780319;Matsuura et al USP 5472883; Stewart et al USP 5561070 Janoff et al USP 4698299; Krillis et al USP 5344758; .

22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terri L Ivory - McCaa whose telephone number is 703-605-1207. The examiner can normally be reached on M-F 8:30-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V Le can be reached on 703-305-3399. The fax phone numbers for

the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

Terri Ivory-McCaa
Patent Examiner
Art Unit 1641
March 26, 2001

Christopher L. Chin

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641